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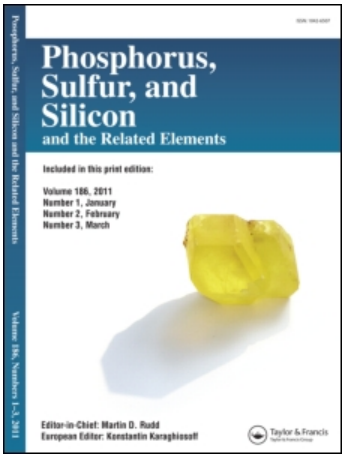

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AN IMPROVED PROCEDURE FOR THE PREPARATION OF N-ARYL SUBSTITUTED 4*H*-1,4-BENZOTHIAZINE 1,1-DIOXIDE DERIVATIVES

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AN IMPROVED PROCEDURE FOR THE PREPARATION OF N-ARYL SUBSTITUTED 4*H*-1,4-BENZOTHIAZINE 1,1-DIOXIDE DERIVATIVES

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An improved procedure for the synthesis of N-aryl substituted 4*H*-1,4-benzothiazine 1,1-dioxide 2-carboxylic acid-esters derivatives is reported. In this new, efficient methodology, silver nitrate was used as a catalyst for the cyclization of N-aryl-phenylsulfonyl-acrylates **6–11** using potassium carbonate in dimethylformamide to the corresponding title compounds in high yields.

Keywords: 4*H*-1,4-Benzothiazine-1,1-dioxide; N-aryl-phenylsulfonylacrylates; silver nitrate; cyclization reaction

INTRODUCTION

An increasing attention for the synthesis of sulfur containing heterocycles has arised in recent years. Perhaps, the most important fact is their use in medicinal and biological chemistry[1–8]. A number of sulfur functionalities such as sulfoxide[1,2], sulfone[2–4] and sulfonamido[5–8] groups are present in biologically active compounds.

4*H*-1,4-benzothiazines have been synthesized by different methods[9–16], most of them leds to structures with an unsubstituted nitrogen atom at position 4 [9–13]. N-alkylated derivatives have been prepared by two meth-

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odologies, the first one, involves the N-alkylation of 4*H*-1,4-benzothiazine 2-carboxylated compounds[14,15]; the second, used in the synthesis of some N-alkyl substituted 2-carboxylic acid 1-oxides, employs a cyclization reaction of their corresponding N-alkyl-phenyl-sulfinyl acrylate precursors with sodium hydride in refluxing toluene, giving poor yields[1]. Trying to find some new 4*H*-1,4-benzothiazine derivatives with possible biological activity, we have recently reported a methodology for the synthesis of some N-aryl substituted 4*H*-1,4-benzothiazine 1,1-dioxide 2-carboxylic acid esters[16]. Although this was the first example of N-aryl derivatives of the 4*H*-1,4-benzothiazine nucleus, the procedure suffers from some disadvantages such as long time period for the key cyclization step and moderate yields. Exploring an alternative cyclization procedure we found that increasing yields were obtained with the aid of silver nitrate as a catalyst, now we present these results.

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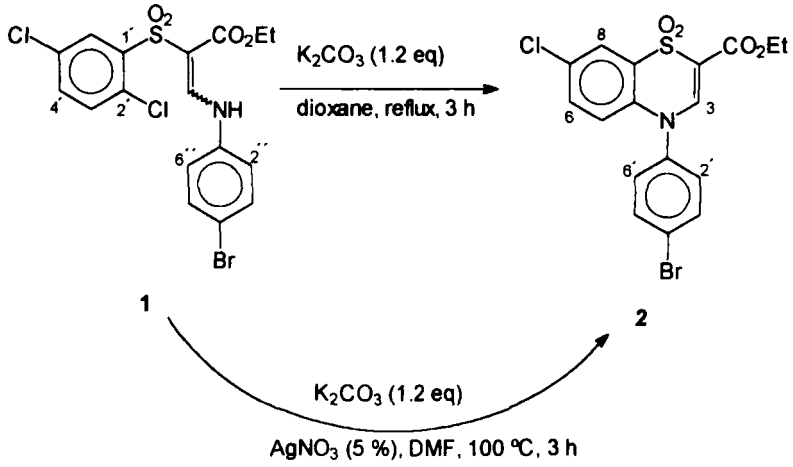
CHEMISTRY

The preparation of N-aryl substituted 4*H*-1,4-benzothiazine 1,1-dioxide 2-carboxylic acid esters **2, 12–17** was accomplished by the synthetic sequence depicted in Schemes 1 and 2. Previously prepared ethyl 2-(2,5-dichloro-phenylsulfonyl)-3-(4-bromoanilino)-acrylate **1** was treated with potassium carbonate (1. 1 eq), silver nitrate (5%) as a catalyst in refluxing dioxane for 3 hours (Scheme 1). Surprisingly, we found a notably enhance in both yield and speed in the cyclization to 4*H*-1,4-benzothiazine sulfone **2** compared with our previous reported methodology, which employs 18-crown-6 as a catalyst[16]. Encouraged by these results, we changed the solvent to the more polar DMF and found complete conversion in an even shorter period of time (reduced from 3 to 2 hours). These later findings were then applied for the synthesis of the desidered N-Aryl 4*H*-1,4-benzothiazine derivatives **12–17** (Scheme 2), and thus employed it for their subsequent synthesis.

Treatment of sodium 2,4-dichlorobenzenesulfinate **3** with ethylbromoacetate in DMF at room temperature for 3 h afforded ethyl 2,4-dichlorophenyl-sulfonylacetate **4**. The reaction of **4** with triethyl orthoformate in acetic anhydride under reflux afforded the enol ether **5**, which, upon evaporation of the solvent to dryness, was allowed to react with a substituted aniline in ethanol under reflux to furnish phenylsulfonyl-acrylates **6–11** as sole prod-



SCHEME 1

ucts. These acrylates were further caused to react with potassium carbonate (1.2 eq) in hot DMF and silver nitrate (5 %) to afford cyclic 4*H*-1,4-benzothiazine derivatives **12–17** in high yields.

RESULTS AND DISCUSSION

Results of the cyclization step are summarized in the Table I. It is well know that halogen substituents can act as donors to very strong Lewis acids[17]. If the complexation process is quite efficient, an enhance in the electronegativity of the donor atom is obtained. This can be favourable in lowering the activation energy in the rate limiting step of the nucleophilic substitution. Recently, it has been found that silver nitrate can act as a catalyst in the heteroaromatic substitution of 2-chloro-quinoxaline using different potassium phenoxy-salts as nucleophiles[18]. These findings aimed us to prove the silver nitrate as a Lewis acid type catalyst in our cyclization reaction. As can be seen, 5% silver nitrate was effective in improving the yield of cyclic **2** in dioxane, obtaining a 68:32 (cyclic:uncyclic) mixture in only 3 hours of reaction. Changing the solvent to DMF, led even to complete cyclization. The ease of this last procedure permitted us the cyclization of the remaining sulfonyl acrylates **6–11** in high yields. In conclusion,

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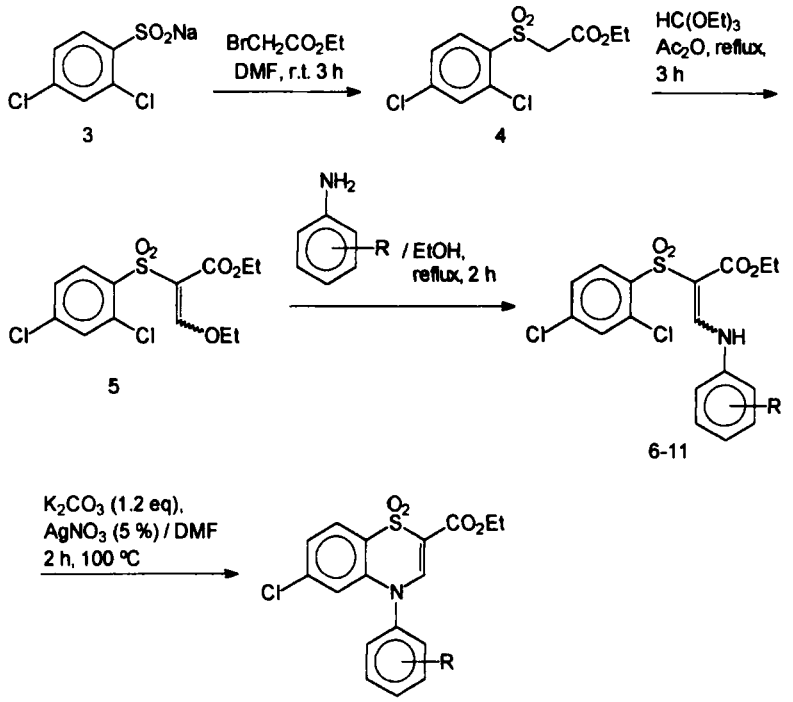

SCHEME 2

we have found an effcient cyclization reaction affording N-aryl substituted 4*H*-1,4-benzothiazines. It opens a better synthetic way for the access of novel derivatives of the 4*H*-1,4-benzothiazine nucleus.

EXPERIMENTAL

Melting points were determined with a Fischer-Johns micro hot-stage apparatus and are uncorrected. The IR spectra were recorded as KBr pellets using a NICOLET Magna-FT/IR 550 spectrometer. Proton NMR spectra (NMR) were recorded on a JEOL Eclipse (270 MHz) spectrometer; δ values in ppm relative to tetramethylsilane are given. When reported, mass spectra were recorded on a Hewlett-Packard HP5971A Mass Selective

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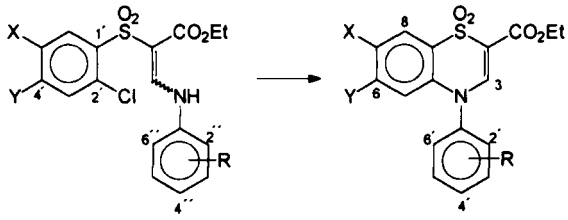
Detector conected to a Gas Chromatograph HP5970 Series II with EI(70 eV). Elemental analysis were performed by Laboratorio de Servicios, Facultad de Ciencias, Escuela de Química, Universidad Central de Venezuela (Caracas, Venezuela); results fill in the range ± 0.4% of the theoretical values. Silica gel plates Merck F_{254} (Merck, Darmstadt, Germany) were used for TLC controls. Column Chromatography was performed with Kiesels gel 60 (70–230 mesh, Merck) and hexane-ethyl acetate (8:2) as eluant. Reagents were obtained from Aldrich (USA) and used without further purification. Solvents were distilled prior to use. Sodium 2,4-dichlorobencenesulfinate **3** was prepared from 2,4-dichloro-benzenesulfonyl chloride [20] following a modification of the methodology described for the preparation of sodium 2,5-dichlorobenzene-sulfinate[19]. Ethyl 2-(2,4-dichloro-phenylsulfonyl)-3-(4-bromoanilino)-acrylate **2** was synthesized according to the literature procedure [16].

TABLE I Cyclic 4H-1,4-benzothiazine derivatives **12** to **17**



No.	*R, X, Y*	*Base, mol-eq.*	*Solvent, catalyst*	*Time(h), temp.*	*Yield (%)*
2	4'-Br, Cl, H	K_2CO_3, 1.2	Dioxane, $AgNO_3$ 5%	3, reflux	52[a]
2	4'-Br, Cl, H	K_2CO_3, 1.2	DMF, $AgNO_3$ 5%	2, 100°C	86
12	4'-Br, H, Cl	K_2CO_3, 1.2	DMF, $AgNO_3$ 5%	2, 100°C	85
13	4'-Cl, H, Cl	K_2CO_3, 1.2	DMF, $AgNO_3$ 5%	2, 100 °C	82
14	3'-Cl, H, Cl	K_2CO_3, 1.2	DMF, $AgNO_3$ 5%	2, 100 °C	80
15	4'-OMe, H, Cl	K_2CO_3, 1.2	DMF, $AgNO_3$ 5%	2, 100 °C	90
16	3'-OMe, H, Cl	K_2CO_3, 1.2	DMF, $AgNO_3$ 5%	2, 100°C	89
17	4'-F, H, Cl	K_2CO_3, 1.2	DMF, $AgNO_3$ 5%	2, 100°C	71

a. Isolated by column chromatography from a 62:38 (cyclic **2** :uncyclic **1**) mixture. Spectroscopic data previously reported [16]

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Sodium 2,4-dichlorobenzenesulfinate 3

A mixture of 2,4-dichloro-benzenesulfonyl-chloride (4.42 g, 18.0 mmol), and sodium sulfite (2.27 g, 18.0 mmol) in water (100 mL) was heated at 80 °C for 2 hours. The solution obtained was allowed to cool at room temperature and was acidified with a 10% solution of hydrochloric acid. The white solid sulfinic acid thus obtained was filtered, washed with cold water and dried under vacuo. Yield: 3.30 g (87 %) *after* recrystallisation from hot water, mp 67–68°C. IR (KBr, cm^{-1}): ν= 2850, 2500 (SO_2H). ^1H NMR ($CDCl_3$/TMS) δ = 5.86 (s, 1H, SO_2H), 7.23–7.30 (m, 2H, 3-H, 5-H), 7.75 (d, 1H, 6-H, J=8.2 Hz).

Anal. Calcd. for $C_6H_4Cl_2O_2S$: C, 34.14; H, 1.91.

Found: C, 34.05; H, 1.89.

For the preparation of sodium 2,4-dichlorobenzenesulfinate **3**, a mixture of 2,4-dichlorobenzenesulfinic acid (3.20 g, 15.18 mmol) and NaOH (0.60 g, 15.18 mmol) in dry ethanol was allowed to react at room temperature for 3 h. The solvent was evaporated under vacuo and the white salt formed used without further purification for the next step.

Ethyl 2,4-dichlorophenyl-sulfonylacetate 4

Sodium 2,4-dichlorobenzenesulfinate **3** (3.50 g, 15.01 mmol) was dissolved in DMF (35 mL), then ethyl bromoacetate (2.50 g, 15.01 mmol) was slowly added and the reaction mixture was stirred at room temperature for 3 h. When the reaction was complete, the mixture was poured into ice-crushed water; the white precipitate formed was filtered, washed twice with water and dried under vacuo, giving a white powder. Yield: 3.21 g (72%) *after* recrystallisation from ethanol, mp 60–61°C. IR (KBr, cm^{-1}): ν = 1730 (C=O, ester); 1340, 1290 (SO_2); 1150, 1100 (SO_2). MS (EI): m/z = 251 (M^+-OC_2H_5). ^1H NMR ($CDCl_3$/TMS): δ = 1.15 (t, 3H, CH_3), 4.09 (c, 2H, O-CH_2-), 4.40 (s, 1H, methylene CH_2), 7.45 (dd, 1H, ar.5′–H, J= 8.4 Hz, J= 2.0 Hz), 7.57 (d, 1H, ar.3′-H, J= 2.0 Hz), 8.04 (d, 1H, ar.6′-H, J= 8.4 Hz).

Anal. Calcd. for $C_{10}H_{10}Cl_2O_4S$: C, 40.42; H, 3.37.

Found: C, 40.35; H, 3.43.

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Ethyl 2-(2,4-dichloro-phenylsulfonyl)-3-(substituted-anilino)-acrylates 6–11

General procedure

A mixture of **4** (2.0 g, 6.73 mmol), acetic anhydride (1.5 g, 10.10 mmol) and triethylorthoformate (1.65 g, 16.15 mmol) was stirred under reflux using a Dean Stark trap for 3 h. The solvent was removed under vacuo and the remaining oil was directly used for the next step. Thus, the oil was dissolved in ethanol (50 mL), treated first dropwise with the substituted aniline (6.73 mmol) and subsequently with 1 drop of concentrated sulfuric acid. The reaction was then stirred under reflux for 2 h and allowed to cool at room temperature. The solid formed was filtered, washed with ethanol, and dried under vacuo to give **6–11**.

Ethyl 2-(2,4-dichloro-phenylsulfonyl)-3-(4-bromoanilino)-acrylate 6

Yield: 2.19 g (68 %) *after* recrystallisation from ethanol, mp: 202–203 °C. IR (KBr, cm^{-1}): $\nu = 3300$ (NH); 1670 (C=O, ester); 1630 (C=C); 1330,1300 (SO_2); 1150,1135 (SO_2). ^1H NMR ($CDCl_3$/TMS): $\delta = 1.09$ (t, 3H, CH_3), 4.08 (c, 2H, CH_2), 7.05 (d, 2H, 2"-H, 6"-H, J= 8.9 Hz), 7.41 (dd, 1H, 5'-H, J=8.4 Hz; J= 2 Hz), 7.45 (d, 1H, 3'-H, J= 2 Hz), 7.52 (d, 2H, 3"-H, 5'-H, J= 8.9 Hz), 8.21 (d, 1H, 6'-H, J= 8.4 Hz), 8.57 (d, 1H, vinyl CH, J= 13.8 Hz), 10.70 (d, 1H, NH, J= 13.8 Hz).

Anal. Calcd. for $C_{17}H_{14}Cl_2BrNO_4S$: C, 40.97; H, 2.81; N, 2.81.

Found: C, 40.86; H, 2.81; N, 2.80

Ethyl 2-(2,4-dichloro-phenyl sulfonyl)-3-(4-chloroanilino)-acrylate 7

Yield: 2.07 g (71 %) *after* recrystallisation from ethanol, mp: 190–191 °C. IR (KBr, cm^{-1}) ν= 3250 (NH); 1670 (C=O, ester); 1625 (C=C); 1325,1300 (SO_2); 1150, 1130 (SO_2). ^1H NMR ($CDCl_3$/TMS): $\delta = 1.09$ (t, 3H, CH_3), 4.09 (c, 2H, CH_2), 7.12(d, 2H, 2"-H, 6"-H, J= 8.9 Hz), 7.37 (d, 2H, 3"-H, 5"-H, J= 8.9 Hz), 7.40 (d, 1H, 3'-H, J= 2.0 Hz), 7.44 (dd, 1H, 5'-H, J= 8.8 Hz, J= 2.0Hz), 8.21 (d, 1H, 6'-H, J= 8.8 Hz), 8.58 (d, 1H, vinyl CH, J= 13.6 Hz), 10.72 (d, 1H, NH, J= 13.6 Hz).

Anal. Calcd. for $C_{17}H_{14}Cl_3NO_4S$: C, 46.99; H, 3.22; N, 3.22.

Found: C, 47.09; H, 3.23; N, 3.21.

Ethyl 2-(2,4-dichloro-phenylsulfonyl)-3-(3-chloroanilino)-acrylate 8

Yield: 2.01 g (69 %) *after* recrystallisation from ethanol, mp: 201–202°C. IR (KBr, cm^{-1}): $\nu = 3300$ (NH); 1675 (C=O, ester); 1620 (C=C); 1340,1310 (SO_2): 1150, 1130 (SO_2). MS (EI): m/z = 433 (M^+). ^1H NMR ($CDCl_3$/TMS): $\delta = 1.10$ (t, 3H, CH_3), 4.12 (c, 2H, CH_2), 7.32–7.46 (m, 3′–H, 5′-H, 2″-H, 4″-H, 5″-H, 6″-H), 8.22 (d, 1H, 6′–H, J = 8.7 Hz), 8.60 (d, 1H, vinyl CH, J= 13.8 Hz), 11.07 (d, 1H, NH, J= 13.8 Hz).

Anal. Calcd. for $C_{17}H_{14}Cl_3NO_4S$: C, 46.99; H, 3.22; N, 3.22

Found: C, 47.06; H, 3.22; N, 3.21

Ethyl 2-(2,4-dichloro-phenylsulfonyl)-3-(4-methoxyanilino)-acrylate 9

Yield: 2.17g (75 %) *after* recrystallisation from ethanol, mp:135–136 °C. IR (KBr, cm^{-1}): $\nu = 3250$ (NH); 1660 (C=O, ester); 1630 (C=C); 1330,1300 (SO_2): 1150,1125 (SO_2). ^1H NMR ($CDCl_3$/TMS): $\delta = 1.09$ (t, 3H, CH_3), 3.81 (s, 3H, OCH_3), 4.10 (c, 2H, CH_2), 6.92 (d, 2H, 2″-H, 6″-H, J= 8.9 Hz), 7.12 (d, 2H, 3″-H, 5″-H, J= 8.9 Hz), 7.40 (dd, 1H, 5′-H, J= 8.4 Hz; J=2 Hz), 7.45 (d, 1H, 3′-H, J= 2.0 Hz), 8.21 (d, 1H, 6′-H, J=8.4 Hz), 8.52 (d, 1H, vinyl CH, J= 13.9 Hz), 10.67 (d, 1H, NH, J= 13.9 Hz).

Anal. Calcd. for $C_{18}H_{17}Cl_2NO_5S$: C, 42.11; H, 3.31; N, 2.73

Found: C, 42.18; H, 3.30; N, 2.74

Ethyl 2-(2,4-dichloro-phenylsulfonyl)-3-(3-methoxyanilino)-acrylate 10

Yield: 2.09 g (72 %) *after* recrystallisation from ethanol, mp: 127–128 °C. IR (KBr, cm^{-1}): $\nu = 3200$ (NH); 1675 (C=O, ester); 1620 (C=C); 1330,1310 (SO_2); 1150,1130 (SO_2). ^1H NMR ($CDCl_3$/TMS): $\delta = 1.09$ (t, 3H, CH_3), 4.08 (c, 2H, CH_2), 3.82 (s, 3H, OCH_3), 6.69–6.77 (m, 3H, 2″-H, 4″-H, 6″-H), 7.29 (dd, 1H, 5″-H, J= 8.1 Hz), 7.40 (dd, 1H, 5′-H, J= 2.0 Hz, J= 8.4 Hz), 7.45 (d, 1H, 3′-H, J= 2.0 Hz), 8.21 (d, 1H, 6′-H, J=8.4 Hz), 8.62 (d, 1H, vinyl CH, J= 13.9 Hz), 10.69 (d, 1H, NH, J= 13.9 Hz).

Anal. Calcd. for $C_{18}H_{17}Cl_2NO_5S$: C, 42.11; H, 3.31: N, 2.73

Found: C, 42.18; H, 3.30; N, 2.74

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Ethyl 2-(2,4-dichloro-phenylsulfonyl)-3-(4-fluoroanilino)-acrylate 11

Yield: 1.83 g (65 %) *after* recrystallisation from ethanol, mp: 163–164 °C. IR (KBr, cm^{-1}) ν = 3300 (NH); 1680 (C=O, ester); 1630 (C=C); 1330, 1310 (SO_2); 1150,1125 (SO_2). ^1H NMR ($CDCl_3$/TMS): δ = 1.08 (t, 3H, CH_3), 4.07 (c, 2H, CH_2), 7.07–7.18 (m, 4H, 2″-H, 3″-H, 5″-H, 6″-H), 7.40 (dd, 1H, 5′-H, J= 2.0 Hz, J= 8.4 Hz), 7.45 (d, 1H, 3′-H, J= 2.0 Hz), 8.21 (d, 1H, 6′-H, J=8.4 Hz), 8.53 (d, 1H, vinyl CH, J= 13.9 Hz), 10.69 (d, 1H, NH, J= 13.9 Hz).

Anal. Calcd. for $C_{17}H_{14}Cl_2FNO_4S$: C, 46.47; H, 3.20; N, 3.20

Found: C, 46.62; H, 3.19; N, 3.20

Ethyl 4-(substituted-aryl)-6-chloro-4*H*-1,4-benzothiazine-2-carboxylate 1,1-dioxides 12–17

General procedure

A mixture of ethyl 2-(2,4-dichloro-phenylsulfonyl)-3-(substituted-anilino)-acrylate **4–9** (3.0 mmol), potassium carbonate (3.6 mmol, 1.2 eq.) and silver nitrate (0.15 mmol, 5 %) in DMF (30 mL) was stirred at 100 °C for 2 hours. Then, the reaction mixture was allowed to stand.at room temperature, filtered and the filtrate liquid poured into crushed ice, the solid thus obtained was filtered, washed with water and dried under vacuo to give **12–17**

Ethyl 4-(4-bromophenyl)-6-chloro-4*H*-1,4-benzothiazine-2-carboxylate 1,1-dioxide 12

Yield: 1.13 g (85 %) *after* recrystallisation from ethanol, mp:247–249°C.; IR (KBr, cm^{-1}): ν = 1700 (C=O, ester); 1620 (C=C); 1280,1270 (SO_2); 1140,1130 (SO_2). ^1H NMR ($CDCl_3$/TMS): δ = 1.39 (t, 3H, CH_3); 4.41 (c, 2H, CH_2); 6.61 (d, 1H, 5-H, J= 1.7 Hz); 7.25 (d, 2H, 2′-H, 6′-H, J= 8.9 Hz); 7.36 (dd, 1H, 7-H, J= 8.6 Hz, J= 1.7 Hz); 7.77 (d, 2H, 3′-H, 5′-H, J= 8.9 Hz); 7.87 (s, 1H, vinyl 3-H); 8.11 (d, 1H, 8-H, J= 8.6 Hz).

Anal. Calcd. for $C_{17}H_{13}ClBrNO_4S$: C, 42.41; H, 2.70; N, 2.91

Found: C, 42.35; H, 2.69; N, 2.90.

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Ethyl 4-(4-chlorophenyl)-6-chloro-4*H*-1,4-benzothiazine-2-carboxylate 1,1-dioxide 13

Yield: 0.98 g (82 %) *after* recrystallisation from ethanol, mp: 223–225 °C; IR (KBr, cm^{-1}) ν = 1690 (C=O, ester); 1625(C=C); 1295, 1280 (SO_2); 1150, 1140 (SO_2). ^1H NMR ($CDCl_3$/TMS): δ = 1.38 (t, 3H, CH_3); 4.38 (c, 2H, CH_2); 6.61 (d, 1H, 5-H, J= 1.7 Hz); 7.32 (d, 2H, 2′-H, 6′-H, J=8.4 Hz); 7.36 (dd, 1H, 7-H, J=8.7 Hz, J= 2.0 Hz), 7.61 (d, 2H, 3′-H, 5′-H, J= 8.4 Hz); 7.87 (s, 1H, vinyl 3-H); 8.10 (d, 1H, 8-H, J= 8.7 Hz).

Anal. Calcd. for $C_{17}H_{13}Cl_2NO_4S$: C, 46.73; H, 2.98; N, 3.20

Found: C, 46.87; H, 2.99; N, 3.21.

Ethyl 4-(3-chlorophenyl)-6-chloro-4*H*-1,4-benzothiazine-2-carboxylate 1,1-dioxide 14

Yield: 0.90 g (76 %) *after* recrystallisation from ethanol, mp: 187–188 °C.; IR (KBr, cm^{-1}): ν = 1690 (C=O, ester); 1620 (C=C); 1290,1270 (SO_2); 1150,1145 (SO_2). MS (EI): m/z= 398 (M^+). ^1H NMR ($CDCl_3$/TMS): δ = 1.30 (t, 3H, CH_3); 4.39 (c, 2H, CH_2); 6.43 (d, 1H, 5-H, J= 2.0 Hz); 7.35–7.41 (m, 3H, 4′-H, 5′-H, 6′-H); 7.53 (dd, 1H, 7-H, J=8.6 Hz, J= 2.0 Hz), 7.70 (d, 1H, 2′-H, J=2.2 Hz),7.74 (s, 1H, vinyl 3-H); 8.11 (d, 1H, 8-H, J= 8.6 Hz).

Anal. Calcd. for $C_{17}H_{13}Cl_2NO_4S$: C, 46.73; H, 2.98; N, 3.20

Found: C, 46.89; H, 2.98; N, 3.21

Ethyl 4-(4-methoxyphenyl)-6-chloro-4*H*-1,4-benzothiazine-2-carboxylate 1,1-dioxide 15

Yield: 1.06 g (90 %) *after* recrystallisation from ethanol, mp: 154–155 °C.; IR (KBr, cm^{-1}): ν = 1690 (C=O, ester); 1623 (C=C); 1300,1287 (SO_2); 1154, 1146 (SO_2). MS (EI): m/z= 393 (M^+). ^1H NMR ($CDCl_3$/TMS): δ = 1.37 (t, 3H, CH_3); 3.89 (s, 3H, OCH_3); 4.37 (c, 2H, CH_2); 6.64 (d, 1H, 5-H, J= 1.7 Hz); 7.07 (d, 2H, 2′-H, 6′-H, J= 8.9 Hz); 7.25 (d, 2H, 3′-H, 5′-H, J= 8.9 Hz); 7.32 (dd, 1H, 7-H, J= 8.6 Hz; J= 1.7 Hz); 7.90 (s, 1H, vinyl 3-H); 8.08 (d, 1H, 8-H, J= 8.6 Hz).

Anal. Calcd. for $C_{18}H_{16}ClNO_5S$: C, 54.89; H, 4.10; N, 3.56

Found: C, 54.68; H, 4.09; N, 3.56

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Ethyl 4-(3-methoxyphenyl)-6-chloro-4*H*-1,4-benzothiazine-2-carboxylate 1,1-dioxide 16

Yield: 1.05 g (89 %) *after* recrystallisation from ethanol, mp: 201–202 °C.; IR (KBr, cm^{-1}): ν = 1690 (C=O, ester); 1623 (C=C); 1300,1287 (SO_2); 1154,1146 (SO_2). MS (EI): m/z= 393 (M^+). ^1H NMR ($CDCl_3$/TMS): δ = 1.39 (t, 3H, CH_3); 3.86 (s, 3H, OCH_3); 4.40 (c, 2H, CH_2); 6.68 (d, 1H, 5-H, J= 1.7 Hz); 6.85 (dd, 1H, 2′-H, J= 2.4 Hz); 6.92 (m, 1H, 6′-H); 7.11 (m, 1H, 4′–H); 7.33 (dd, 1H, 7-H, J=8.6 Hz; J=1.7 Hz); 7.51 (dd, 1H, 5′-H, J=8.2 Hz), 7.92 (s, 1H, vinyl 3-H); 8.09 (d, 1H, 8-H, J= 8.6 Hz).

Anal. Calcd. for $C_{18}H_{16}ClNO_5S$: C, 54.89; H, 4.10; N, 3.56

Found: C, 54.68; H, 4.09; N, 3.56

Ethyl 4-(4-fluorophenyl)-6-chloro-4*H*-1,4-benzothiazine-2-carboxylate 1,1-dioxide 17

Yield: 0.81 g (71 %) *after* recrystallisation from ethanol, mp: 188–190 °C.; IR (KBr, cm^{-1}): ν = 1695 (C=O, ester); 1620 (C=C); 1295,1283 (SO_2); 1149, 1138 (SO_2). ^1H NMR ($CDCl_3$/TMS): δ = 1.39 (t, 3H, CH_3); 4.42(c, 2H, CH_2); 6.58(d, 1H, 5-H, J=8.9 Hz); 7.29–7.39 (m, 5H, arom., 2′–H, 3′-H, 5′-H, 6′–H, 6-H); 7.88 (s, 1H, vinyl 3-H); 8.13 (d, 1H, 8′-H, J= 2.5 Hz).

Anal. Calcd. for $C_{17}H_{13}ClFNO_4S$: C, 53.48; H, 3.43; N, 3.67

Found: C, 53.60; H, 3.44; N, 3.66

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